

NMCP COVID-19 Literature Report #69: Friday, 04 June 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

TABLE OF CONTENTS

Topic page; click link to jump to section. References can be found on the [website](#).

The Big Picture	2	Pediatric Population	26
SARS-CoV-2 Virus and Variants	5	Impact on Healthcare Workers	30
Vaccines and Vaccine Hesitancy	8	Mental Health and Wellness	32
Treatments and Management	15	Disparities and Health Equity	34
Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases	20	Risk, Transmission, Exposure, and Testing	38
Long COVID / Post-COVID Period	23	Reinfections, Coinfections, and Other Infectious Diseases	42
Women's Health, Pregnancy, and Perinatal Care	24	Statistics	47

The Big Picture

News in Brief

"The 'time has come' for a global pandemic treaty, WHO's Tedros says" ([NPR](#)).

"A clue to why the 1918 pandemic came back stronger than before: Three 103-year-old-lung samples hinted at how the flu mutated to become more deadly" ([Atlantic](#)).

The Lab Leak Theory

"Biden asks intelligence community to redouble efforts to determine definitive origin of the coronavirus" ([WP](#)).

"Divisive COVID 'lab leak' debate prompts dire warnings from researchers: Allegations that COVID escaped from a Chinese lab make it harder for nations to collaborate on ending the pandemic — and fuel online bullying, some scientists say" ([Nature](#); see also: letter from researcher published in [Science](#)).

"If the lab-leak theory is right, what's next? We know enough to acknowledge that the scenario is possible, and we should therefore act as though it's true" ([Atlantic](#)).

"Timeline: How the Wuhan lab-leak theory suddenly became credible" ([WP](#)).

"Search for origin of COVID-19 'poisoned by politics', says WHO expert" ([Reuters](#)).

Perspective: "We may never know where the virus came from. But evidence still suggests nature: Labs like the one in Wuhan are essential to preparing for future pandemics" ([WP](#)).

Webinars and Conferences

WHAT: WHO global conference on communicating science during health emergencies (open plenary)

WHEN: Monday, 07 June 2021, 0700-1000 (New York)

DETAILS: "Many good practice examples of science communication have already emerged during the COVID-19 pandemic. These innovative solutions represent a valuable resource for the current and future health emergencies. The World Health Organization Information Network for Epidemics (WHO EPI-WIN) plans to organize its first global ad hoc conference on communicating science during public health emergencies to facilitate the solution-oriented discussion of challenges and best practices in health science communication during the COVID-19 pandemic. The insights of the conference will eventually contribute to a repository of best practices and feed into the development of standards for

effective science communication during health emergencies. The conference will further recognize innovative science communication concepts in the areas of (i) science communication for researchers, (ii) science and the media, and (iii) translating science into action."

REGISTER: https://who.zoom.us/webinar/register/WN_I5xrw5G6QA0YZh4jeQ6wxQ

WHAT: Virtual Summer Workshop on Pandemics and Global Health Security

WHEN: 19-21 July 2021, 0900-1230 ET daily

DETAILS: "COVID-19 has exposed just how unprepared governments, corporations, and societies are for a global pandemic. While the SARS-CoV-2 virus is only the most recent threat to global health security, it will certainly not be the last. Threats to global health security continue to evolve due to the emergence of new infectious diseases, globalization, advances in science and technology, and the changing nature of conflict.

Pandemics and Global Health Security is a three-day virtual, non-credit workshop designed to introduce participants to the challenges facing the world at the intersection of pandemic preparedness and response, public health, national security, and the life sciences. Over the course of three days, participants will discuss how the biology and epidemiology of SARS-CoV-2 contributed to the emergence of that virus as a global pandemic, lessons learned from Operation Warp Speed about the development of medical countermeasures, obstacles to hospital biopreparedness, challenges to science communication during a pandemic, the bioethics of resource allocation during a public health emergency, the future of global health security, and the role of science and technology in preventing and responding to pandemics. The workshop faculty are internationally recognized experts from the government, private sector, and academia who have been extensively involved in research and policy-making on public health, biodefense, and security issues. The workshop is organized by the Biodefense Graduate Program at the Schar School of Policy and Government at George Mason University and will be held virtually on July 19-21, 2021. Each day will run from 9am to 12:30pm ET."

COST: \$400 early bird rate available until 18 June 2021, then \$500

REGISTER: <https://schar.sitemasonry.gmu.edu/programs/executive-education/summer-workshop-pandemics-and-global-health-security>

Peer-Reviewed Articles

Clin Infect Dis: [Risk Factors for Death Among the First 80 543 COVID-19 Cases in China: Relationships Between Age, Underlying Disease, Case Severity, and Region](#) (27 May 2021)

"Knowledge of COVID-19 epidemiology remains incomplete and crucial questions persist. We aimed to examine risk factors for COVID-19 death.

A total of 80 543 COVID-19 cases reported in China, nationwide, through April 8, 2020 were included. Risk factors for death were investigated by Cox proportional hazards regression and stratified analyses.

Overall national case fatality ratio (CFR) was 5.64%. Risk factors for death were older age (≥ 80 : adjusted hazard ratio [aHR]=12.58, 95% confidence interval [CI]=6.78-23.33), presence of underlying disease (aHR=1.33, CI=1.19-1.49), worse case severity (severe: aHR=3.86, CI=3.15-4.73; critical: aHR=11.34, CI=9.22-13.95), and near-epicenter region (Hubei: aHR=2.64, CI=2.11-3.30; Wuhan: aHR=6.35, CI=5.04-8.00). CFR increased from 0.35% (30-39 years) to 18.21% (≥ 70 years) without underlying disease. Regardless of age, CFR increased from 2.50% for no underlying disease to 7.72% for 1, 13.99% for 2, and 21.99% for ≥ 3 . CFR increased with worse case severity from 2.80% (mild), to 12.51% (severe) and 48.60% (critical) regardless of region. Compared to other regions, CFR was much higher in Wuhan regardless of case severity (mild: 3.83% versus 0.14% in Hubei and 0.03% elsewhere; moderate: 4.60% versus 0.21% and 0.06%; severe: 15.92% versus 5.84% and 1.86%; and critical: 58.57% versus 49.80% and 18.39%).

Older patients regardless of underlying disease and patients with underlying disease regardless of age were at elevated risk of death. Higher death rates near the outbreak epicenter and during the surge of cases reflect the deleterious effects of allowing health systems to become overwhelmed."

PLoS Med: [COVID-19 and excess mortality in the United States: A county-level analysis](#) (20 May 2021)

"Why was this study done?

- > The Coronavirus Disease 2019 (COVID-19) pandemic has resulted in excess mortality that would not have occurred in the absence of the pandemic.
- > Excess deaths include deaths assigned to COVID-19 in official statistics as well as deaths that are not assigned to COVID-19 but are attributable directly or indirectly to COVID-19.
- > While prior studies have identified significant racial and socioeconomic inequities in directly assigned COVID-19 deaths, few studies have documented how excess mortality in 2020 has differed across sociodemographic or health factors in the United States.

What did the researchers do and find?

- > Leveraging data from 2,096 counties on COVID-19 and all-cause mortality, we assessed what percentage of excess deaths were not assigned to COVID-19 and examined variation in excess deaths by county characteristics.
- > In these counties, we found that for every 100 deaths directly assigned to COVID-19 in official statistics, an additional 20 deaths occurred that were not counted as direct COVID-19 deaths.
- > The proportion of excess deaths not counted as direct COVID-19 deaths was even higher in counties with lower average socioeconomic status, counties with more comorbidities, and counties in the South and West. Counties with more non-Hispanic Black residents, who were already at high risk of COVID-19 death based on direct counts, also reported a higher proportion of excess deaths not assigned to COVID-19.

What do these findings mean?

- > Direct COVID-19 death counts significantly underestimate excess mortality in 2020.
- > Monitoring excess mortality will be critical to gain a full picture of socioeconomic and racial inequities in mortality attributable to the COVID-19 pandemic.
- > To prevent inequities in mortality from growing even larger, health equity must be prioritized in the policy response to the COVID-19 pandemic."

SARS-CoV-2 Virus and Variants

News in Brief

The WHO will now use letters of the Greek alphabet to simplify the names of coronavirus strains (and destigmatize geographic references), based on order they emerged – the UK variant will be alpha, the Indian variant called delta, etc. ([WHO](#); see [website](#) for 'conversion' and tracking).

"India asks social media firms to remove reference to 'Indian variant' of coronavirus" ([Reuters](#)).

"What scientists know about new, fast-spreading coronavirus variants: Key questions remain about how quickly B.1.617 variants can spread, their potential to evade immunity and how they might affect the course of the pandemic" ([Nature](#)).

"The mini lungs and other organoids helping to beat COVID: Virologists have infected millions of miniature organs with SARS-CoV-2, to learn how the virus wreaks havoc and how to stop it" ([Nature](#)).

Webinars

- WHAT: COVID-19 Conversations: Variants and Vaccines Presented by the American Public Health Association (APHA) and National Academy of Medicine (NAM)
- DETAILS: "The 18th COVID-19 Conversations webinar focused on emerging COVID-19 variants, how vaccines can adapt to these new variants, and other interventions that could help curb transmission."
- WEBSITE: <https://covid19conversations.org/Webinars/variants> – includes links to presenter slides, transcript, and recording [YouTube]

Peer-Reviewed Articles

Nature: [Nasal delivery of an IgM offers broad protection from SARS-CoV-2 variants](#) (03 June 2021)

"Resistance represents a major challenge for antibody-based therapy for coronavirus disease 2019 (COVID-19)1–4. Here we engineered an immunoglobulin M (IgM) neutralizing antibody (IgM-14) to overcome the resistance encountered by IgG-based therapeutics. IgM-14 is >230-fold more potent than its parental IgG-14 in neutralizing the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). IgM-14 potently neutralizes the resistant virus raised by its corresponding IgG-14, the newly emerged United Kingdom B.1.1.7, Brazilian P.1, and South African B.1.351 variants of concern (VOCs), and 21 other receptor-binding domain (RBD) mutants, many of which are resistant to the IgGs that have been authorized for emergency use. Although engineering IgG into IgM enhances antibody potency in general, selection of an optimal epitope is critical for identifying the most effective IgM that can overcome resistance. One single intranasal (IN) dose of 0.044 and 0.4 mg/kg IgM-14 confers prophylactic and therapeutic efficacy against SARS-CoV-2 in mice, respectively. IgM-14, but not IgG-14, also confers potent therapeutic protection against the P.1 and B.1.351 variants. IgM-14 exhibits desirable IN pharmacokinetics and safety in rodents. Our results demonstrate that IN administration of an engineered IgM can improve efficacy, reduce resistance, and simplify the prophylactic and therapeutic treatment of COVID-19."

Transfusion: [Minipool testing for SARS-CoV-2 RNA in United States blood donors](#) (27 May 2021)

"SARS-CoV-2 RNA prevalence in blood donors from large geographic areas of high community transmission is limited. We tested residual donor plasma minipools (MPs) to determine SARS-CoV-2 RNAemia prevalence in six United States areas.

Blood donations collected from 7 March 2020 to 25 September 2020 were tested for SARS-CoV-2 RNA (vRNA) in MP of 6 or 16 donations using the Grifols Procleix SARS-CoV-2

research-use only (RUO) transcription-mediated amplification (TMA) assay. Reactive results were confirmed using an alternate target region TMA assay. Reactive MPs were tested by TMA after serial dilution to estimate viral load. Testing for anti-SARS-CoV-2 antibodies and infectivity was performed.

A total of 17,995 MPs corresponding to approximately 258,000 donations were tested for vRNA. Three confirmed reactive MP16 were identified. The estimated prevalence of vRNA reactive donations was 1.16/100,000 (95% CI 0.40, 3.42). The vRNA-reactive samples were non-reactive for antibody, and the estimated viral loads of the (presumed single) positive donations within each MP ranged from <1000 to <4000 copies/ml. When tested, no infectivity was observed in inoculated permissive cell cultures.

Blood donation MP-nucleic acid testing (NAT) indicated that SARS-CoV-2 RNAemia is infrequent and, when detected, the vRNA was at low concentrations. Only one RNA-reactive MP could be tested for infectivity for operational reasons and was not infectious in cell culture. These findings support current recommendations from international and national regulatory agencies to not screen donors by NAT."

Nature: [SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans](#) (24 May 2021)

"Long-lived bone marrow plasma cells (BMPCs) are a persistent and essential source of protective antibodies^{1–7}. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) convalescent individuals have a significantly lower risk of reinfection^{8–10}. Nonetheless, it has been reported that anti-SARS-CoV-2 serum antibodies experience rapid decay in the first few months after infection, raising concerns that long-lived BMPCs may not be generated and humoral immunity against this virus may be short-lived^{11–13}. Here we demonstrate that in patients who experienced mild infections (n=77), serum anti-SARS-CoV-2 spike (S) antibodies decline rapidly in the first 4 months after infection and then more gradually over the following 7 months, remaining detectable at least 11 months after infection. Anti-S antibody titers correlated with the frequency of S-specific BMPCs obtained from bone marrow aspirates of 18 SARS-CoV-2 convalescent patients 7 to 8 months after infection. S-specific BMPCs were not detected in aspirates from 11 healthy subjects with no history of SARS-CoV-2 infection. We demonstrate that S-binding BMPCs are quiescent, indicating that they are part of a long-lived compartment. Consistently, circulating resting memory B cells directed against the S protein were detected in the convalescent individuals. Overall, we show that SARS-CoV-2 infection induces a robust antigen-specific, long-lived humoral immune response in humans."

See also: [bioRxiv preprint - Naturally enhanced neutralizing breadth to SARS-CoV-2 after one year](#)

Cell Metab: [SARS-CoV-2 infects human pancreatic \$\beta\$ cells and elicits \$\beta\$ cell impairment](#) (18 May 2021)

"Highlights:

- SARS-CoV-2 infects β cells in COVID-19 patients and human islets in vitro
- SARS-CoV-2 infection causes β cell death and reduced GSIS in vitro
- Phosphoproteomics shows SARS-CoV-2 spike protein and virus induce apoptotic kinases
- High neuropilin-1 levels support β cell selectivity, and inhibitors block infection"

Vaccines and Vaccine Hesitancy

News in Brief

Finally, a positive milestone: As of 25 May 2021 (and less than 6 months since vaccines were first available), half of US adults are fully vaccinated against COVID-19 ([NPR](#)).

12 states – VT, HI, MA, CT, ME, NJ, RI, NM, PA, NH, MD, and CA – are at 70% of adult population with a first dose of a COVID-19 vaccine, with 10 more states above 65% ([Twitter](#)).

"C.D.C. is investigating a heart problem in a few young vaccine recipients" ([NYT](#); see also: [CDC's VaST Work Group report from 17 May 2021](#)).

Moderna is initiating the first steps for its coronavirus vaccine to get the FDA's approval beyond EUA ([Moderna](#)).

Research Efforts

Pfizer is looking at combining the pneumococcal vaccine with a COVID-19 booster ([Reuters](#)).

And the NIH is starting a trial to evaluate mixed vaccine schedules ([NIH](#)).

"Scientists zero in on long-sought marker of COVID-vaccine efficacy: Data from seven vaccination trials help to identify a blood marker for protection against the disease" ([Nature](#)).

Avoiding the Needle

Some researchers suggest that COVID-19 survivors only need one dose of a vaccine ([EBioMedicine](#)).

Want to avoid the needle completely? A vaccine patch could be in our future ([NPR](#)).

Long read: "What makes injections hard to swallow? An anthropological assessment of the differences between pills and injections may shed some light on vaccine hesitancy" ([Sapiens](#)).

Supply and Demand

Another COVID-19 vaccine could start production within weeks ([AP](#)).

"The 6 reasons Americans aren't getting vaccinated" ([Vox](#)).

What if it's apathy and not hesitancy that is driving vaccine disinterest? ([JAMA](#))

Vaccine Messaging

"'It's a minefield': COVID vaccine safety poses unique communication challenge: Poll on vaccine hesitancy demonstrates the extraordinary predicament researchers face in transmitting risk information during a pandemic" ([Nature](#)).

"These are the text messages that get people to take vaccines: Lotteries and cash payouts are getting lots of attention. But smaller nudges work, too" ([WP](#)).

Special Reports and Other Resources

RF: [One for All: An Updated Action Plan for Global Covid-19 Vaccination](#) (June 2021)

"The continued spread of the SARS-CoV-2 virus in unvaccinated populations threatens to keep the global economy choked for the foreseeable future and poses threats to current progress in containing the pandemic. Stopping the spread of this pandemic requires that all countries have equal access to Covid-19 vaccination. But currently, there is a major disparity in vaccine distribution.

- Nearly 50 percent of North Americans have been vaccinated, more than 25 percent of Europeans, about 14 percent of South Americans, but only 5 percent of Asians, and 1.2 percent of Africans
- More than 80 percent of shots have gone into arms in high- and upper-middle income countries leaving the pandemic to spread unchecked in lower-income countries and at risk of continually reigniting a global Covid-19 spread and continued mutations in the virus.

The inequity and the lack of a strong global vaccination campaign extend beyond a health crisis. Our interconnected global economy stands to lose as much as US\$9.2 trillion if governments fail to ensure developing economy access to Covid-19 vaccines.

This update of the first report in April 2021, offers a 5-point action plan to scale equitable vaccination around the world: (1) Share more sooner; (2) Make more quicker; (3) Build in the global South' (4) Support delivery systems; and (5) Close the financing gap."

Peer-Reviewed Articles

NEJM: [Thromboembolic Events in the South African Ad26.COV2.S Vaccine Study](#) (02 June 2021)

In this South African trial of Johnson & Johnson's COVID shot, thromboembolic events were seen in five health workers with known risk factors, but there were no cases of vaccine-induced immune thrombotic thrombocytopenia.

Clin Infect Dis: [Neutralization heterogeneity of United Kingdom and South-African SARS-CoV-2 variants in BNT162b2-vaccinated or convalescent COVID-19 healthcare workers](#) (29 May 2021)

"There are concerns about neutralizing antibodies (NABs) potency against SARS-CoV-2 variants. Despite decreased NAb titers elicited by BNT162b2-vaccine against VOC202012/01 and 501Y.V2 strains, 28/29 healthcare workers (HCW) had a NAb titer $\geq 1:10$. In contrast, six months after COVID-19 mild-forms, only 9/15 (60%) of HCW displayed detectable NABs against 501Y.V2 strain."

J Infect: [Previous COVID-19 infection, but not Long-COVID, is associated with increased adverse events following BNT162b2/Pfizer vaccination](#) (28 May 2021)

Letter to the editor; summary from [CIDRAP](#):

"An increased risk of adverse events after the first Pfizer/BioNTech COVID-vaccine dose was associated with previous COVID-19 infection, according to a letter to the editor late last week in the Journal of Infection.

The researchers surveyed 974 UK healthcare workers (mean age, 48.9 years) who received their first dose of the Pfizer vaccine. One in four (27.2%) had a previous positive PCR or antibody test result, and 30 of them said they were experiencing long COVID (median duration, 9.3 months).

Female sex and younger age were associated with increased risk of COVID-19 vaccination adverse events, but data also showed that those with previous COVID infections were associated with more vaccine symptoms (1.61 vs 0.89) and vaccine symptom severity (2.7 vs 1.5 symptom-days) after adjustments were made for age and sex. The most common symptoms were fever, fatigue, muscle pain, joint pain, and lymph node pathology. Long COVID-19 was not linked with an increase in adverse events post-vaccination.

"Importantly, among those with prior COVID-19, there was no significant relationship between illness-vaccine time interval and other composite score [of symptom nature and severity]," write the researchers, "nor any difference in mean time interval based on presence of any of the symptoms.""

MMWR: [Patterns in COVID-19 Vaccination Coverage, by Social Vulnerability and Urbanicity — United States, December 14, 2020–May 1, 2021](#) (28 May 2021)

"What is already known about this topic? Counties with higher levels of social vulnerability have been disproportionately affected by COVID-19.

What is added by this report? Disparities in county-level vaccination coverage by social vulnerability have increased as vaccine eligibility has expanded, especially in large fringe metropolitan (areas surrounding large cities, e.g., suburban) and nonmetropolitan counties. By May 1, 2021, vaccination coverage among adults was lower among those living in counties with lower socioeconomic status and with higher percentages of households with children, single parents, and persons with disabilities.

What are the implications for public health practice? Outreach efforts, including expanding public health messaging tailored to local populations and increasing vaccination access, could help increase vaccination coverage in counties with high social vulnerability."

MMWR: [COVID-19 Vaccine Breakthrough Infections Reported to CDC — United States, January 1–April 30, 2021](#) (28 May 2021)

"A total of 10,262 SARS-CoV-2 vaccine breakthrough infections had been reported from 46 U.S. states and territories as of April 30, 2021. Among these cases, 6,446 (63%) occurred in females, and the median patient age was 58 years (interquartile range = 40–74 years). Based on preliminary data, 2,725 (27%) vaccine breakthrough infections were asymptomatic, 995 (10%) patients were known to be hospitalized, and 160 (2%) patients died....

Beginning May 1, 2021, CDC transitioned from monitoring all reported COVID-19 vaccine breakthrough infections to investigating only those among patients who are hospitalized or die, thereby focusing on the cases of highest clinical and public health significance. CDC will continue to lead studies in multiple U.S. sites to evaluate vaccine effectiveness and collect information on all COVID-19 vaccine breakthrough infections regardless of clinical status. Additional information and resources to help public health departments and laboratories investigate and report COVID-19 vaccine breakthrough cases are available at <https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html>."

See also: "CDC move to limit investigations into COVID breakthrough infections sparks concerns" ([NPR](#)).

NEJM: [Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents](#) (27 May 2021)

"In this ongoing multinational, placebo-controlled, observer-blinded trial, we randomly assigned participants in a 1:1 ratio to receive two injections, 21 days apart, of 30 µg of

BNT162b2 or placebo. Noninferiority of the immune response to BNT162b2 in 12-to-15-year-old participants as compared with that in 16-to-25-year-old participants was an immunogenicity objective. Safety (reactogenicity and adverse events) and efficacy against confirmed coronavirus disease 2019 (Covid-19; onset, ≥ 7 days after dose 2) in the 12-to-15-year-old cohort were assessed.

Overall, 2260 adolescents 12 to 15 years of age received injections; 1131 received BNT162b2, and 1129 received placebo. As has been found in other age groups, BNT162b2 had a favorable safety and side-effect profile, with mainly transient mild-to-moderate reactogenicity (predominantly injection-site pain [in 79 to 86% of participants], fatigue [in 60 to 66%], and headache [in 55 to 65%]); there were no vaccine-related serious adverse events and few overall severe adverse events. The geometric mean ratio of SARS-CoV-2 50% neutralizing titers after dose 2 in 12-to-15-year-old participants relative to 16-to-25-year-old participants was 1.76 (95% confidence interval [CI], 1.47 to 2.10), which met the noninferiority criterion of a lower boundary of the two-sided 95% confidence interval greater than 0.67 and indicated a greater response in the 12-to-15-year-old cohort. Among participants without evidence of previous SARS-CoV-2 infection, no Covid-19 cases with an onset of 7 or more days after dose 2 were noted among BNT162b2 recipients, and 16 cases occurred among placebo recipients. The observed vaccine efficacy was 100% (95% CI, 75.3 to 100).

The BNT162b2 vaccine in 12-to-15-year-old recipients had a favorable safety profile, produced a greater immune response than in young adults, and was highly effective against Covid-19."

JAMA: [Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial](#) (26 May 2021)

"This interim analysis of an ongoing randomized trial evaluates the efficacy of 2 inactivated coronavirus vaccines for preventing symptomatic COVID-19 in healthy adults and adverse events after immunization....

Question What is the efficacy of 2 inactivated SARS-CoV-2 vaccines for prevention of symptomatic COVID-19?

Findings This prespecified interim analysis of a randomized clinical trial included 40 382 participants who received at least 1 dose of a 2-dose inactivated vaccine series developed from either SARS-CoV-2 WIV04 (5 $\mu\text{g}/\text{dose}$) or HB02 (4 $\mu\text{g}/\text{dose}$) strains or an aluminum hydroxide-only control, with a primary end point of the incidence of symptomatic COVID-19 at least 14 days after the second injection. The efficacy for the 2 vaccines, compared with an aluminum hydroxide-only control, was 72.8% in the WIV04 group and 78.1% in the HB02 group; both comparisons were statistically significant.

Meaning Two inactivated SARS-CoV-2 vaccines demonstrated efficacy against symptomatic COVID-19 compared with an aluminum hydroxide-only control."

Emerg Infect Dis: [Multisystem Inflammatory Syndrome after SARS-CoV-2 Infection and COVID-19 Vaccination](#) (25 May 2021)

"We report 3 patients in California, USA, who experienced multisystem inflammatory syndrome (MIS) after immunization and severe acute respiratory syndrome coronavirus 2 infection. During the same period, 3 adults who were not vaccinated had MIS develop at a time when $\approx 7\%$ of the adult patient population had received >1 vaccine."

JAMA: [Public Trust and Willingness to Vaccinate Against COVID-19 in the US From October 14, 2020, to March 29, 2021](#) (24 May 2021)

"This online survey study of US adults characterizes trends in coronavirus vaccine hesitancy and public trust in vaccination before and after COVID-19 vaccine availability in the US."

PLoS One: [Factors indicating intention to vaccinate with a COVID-19 vaccine among older U.S. adults](#) (24 May 2021)

"The success of vaccination efforts to curb the COVID-19 pandemic will require broad public uptake of immunization and highlights the importance of understanding factors associated with willingness to receive a vaccine.

U.S. adults aged 65 and older enrolled in the Heartline™ clinical study were invited to complete a COVID-19 vaccine assessment through the Heartline™ mobile application between November 6–20, 2020. Factors associated with willingness to receive a COVID-19 vaccine were evaluated using an ordered logistic regression as well as a Random Forest classification algorithm.

Among 9,106 study participants, 81.3% ($n = 7402$) responded and had available demographic data. The majority (91.3%) reported a willingness to be vaccinated. Factors most strongly associated with vaccine willingness were beliefs about the safety and efficacy of COVID-19 vaccines and vaccines in general. Women and Black or African American respondents reported lower willingness to vaccinate. Among those less willing to get vaccinated, 66.2% said that they would talk with their health provider before making a decision. During the study, positive results from the first COVID-19 vaccine outcome study were released; vaccine willingness increased after this report.

Even among older adults at high-risk for COVID-19 complications who are participating in a longitudinal clinical study, 1 in 11 reported lack of willingness to receive COVID-19 vaccine in November 2020. Variability in vaccine willingness by gender, race, education, and income suggests the potential for uneven vaccine uptake. Education by health providers directed

toward assuaging concerns about vaccine safety and efficacy can help improve vaccine acceptance among those less willing."

Clin Infect Dis: [Circulating SARS-CoV-2 Vaccine Antigen Detected in the Plasma of mRNA-1273 Vaccine Recipients](#) (20 May 2021)

"SARS-CoV-2 proteins were measured in longitudinal plasma samples collected from 13 participants who received two doses of mRNA-1273 vaccine. 11 of 13 participants showed detectable levels of SARS-CoV-2 protein as early as day one after first vaccine injection. Clearance of detectable SARS-CoV-2 protein correlated with production of IgG and IgA."

Vaccines: [Effect of Information about COVID-19 Vaccine Effectiveness and Side Effects on Behavioural Intentions: Two Online Experiments](#) (13 April 2021)

The success of mass COVID-19 vaccination campaigns rests on widespread uptake. However, although vaccinations provide good protection, they do not offer full immunity and while they likely reduce transmission of the virus to others, the extent of this remains uncertain. This produces a dilemma for communicators who wish to be transparent about benefits and harms and encourage continued caution in vaccinated individuals but not undermine confidence in an important public health measure.

In two large pre-registered experimental studies on quota-sampled UK public participants we investigate the effects of providing transparent communication—including uncertainty—about vaccination effectiveness on decision-making.

In Study 1 (n = 2097) we report that detailed information about COVID-19 vaccines, including results of clinical trials, does not have a significant impact on beliefs about the efficacy of such vaccines, concerns over side effects, or intentions to receive a vaccine.

Study 2 (n = 2217) addressed concerns that highlighting the need to maintain protective behaviours (e.g., social distancing) post-vaccination may lower perceptions of vaccine efficacy and willingness to receive a vaccine.

We do not find evidence of this: transparent messages did not significantly reduce perceptions of vaccine efficacy, and in some cases increased perceptions of efficacy. We again report no main effect of messages on intentions to receive a vaccine. The results of both studies suggest that transparently informing people of the limitations of vaccinations does not reduce intentions to be vaccinated but neither does it increase intentions to engage in protective behaviours post-vaccination."

Treatments and Management

News in Brief

The NIH has updated its COVID-19 treatment guidelines: it recommends using either baricitinib or tocilizumab with dexamethasone alone or plus remdesivir for hospitalized patients on high-flow oxygen or noninvasive ventilation who have clinical progression or elevated inflammation markers ([NIH](#)).

The FDA has given EUA to sotrovimab, a monoclonal antibody, for mild to moderate COVID-19 in patients 12 years and older ([FDA](#)).

"NIH researchers identify potential new antiviral drug for COVID-19" ([NIH](#); see also: [full text article on study](#)).

Peer-Reviewed Articles

J Antimicrob Chemother: [Concordance between the results of randomized and non-randomized interventional clinical trials assessing the efficacy of drugs for COVID-19: a cross-sectional study](#) (02 June 2021)

"To assess whether results of observational studies of potential anti-COVID-19 drugs were reproduced in subsequent randomized controlled trials (RCTs).

This was a retrospective cross-sectional study, including studies published online between 1 January and 27 October 2020 that evaluated potential COVID-19 treatments and reported all-cause mortality.

Of 133 comparisons included in 117 studies, most were non-randomized (104/133, 78%). Hydroxychloroquine was the most common drug type, combined with azithromycin (n = 27, 20%) or alone (n = 22, 16%), followed by IL-6 inhibitors (n = 36, 27%) and corticosteroids (n = 26, 20%). Seventy-one percent (74/104) of non-randomized studies reported adjusted survival results and only 8% (8/104) adjusted for immortal time bias. Only two RCTs (2/29, 7%) reported significant survival benefit, both reporting treatment with corticosteroids, while 32/104 (31%) non-randomized studies showed statistically significant survival benefit associated with the intervention arm. The results of the majority (28/32, 88%) of non-randomized studies reporting survival benefit were not replicated by large-scale RCTs.

The results of most non-randomized studies reporting survival benefit of potential anti-COVID-19 drugs were not replicated by large RCTs. Regulators and healthcare professionals should exercise caution and resist the pressure to approve and prescribe drugs of unproven efficacy and potential toxicity to optimize patient care and maintain public trust in medical science."

BMC Infect Dis: [Reducing the use of empiric antibiotic therapy in COVID-19 on hospital admission](#) (02 June 2021)

"Empiric antibiotics for community acquired bacterial pneumonia (CABP) are often prescribed to patients with COVID-19, despite a low reported incidence of co-infections. Stewardship interventions targeted at facilitating appropriate antibiotic prescribing for CABP among COVID-19 patients are needed. We developed a guideline for antibiotic initiation and discontinuation for CABP in COVID-19 patients. The purpose of this study was to assess the impact of this intervention on the duration of empiric CABP antibiotic therapy among patients with COVID-19.

This was a single-center, retrospective, quasi-experimental study of adult patients admitted between 3/1/2020 to 4/25/2020 with COVID-19 pneumonia, who were initiated on empiric CABP antibiotics. Patients were excluded if they were initiated on antibiotics > 48 h following admission or if another source of infection was identified. The primary outcome was the duration of antibiotic therapy (DOT) prior to the guideline (March 1 to March 27, 2020) and after guideline implementation (March 28 to April 25, 2020). We also evaluated the clinical outcomes (mortality, readmissions, length of stay) among those initiated on empiric CABP antibiotics.

A total of 506 patients with COVID-19 were evaluated, 102 pre-intervention and 404 post-intervention. Prior to the intervention, 74.5% (n = 76) of patients with COVID-19 received empiric antibiotics compared to only 42% of patients post-intervention (n = 170), $p < 0.001$. The median DOT in the post-intervention group was 1.3 days shorter ($p < 0.001$) than the pre-intervention group, and antibiotics directed at atypical bacteria DOT was reduced by 2.8 days ($p < 0.001$). More patients in the post-intervention group were initiated on antibiotics based on criteria consistent with our guideline (68% versus 87%, $p = 0.001$). There were no differences between groups in terms of clinical outcomes.

Following the implementation of a guideline outlining recommendations for initiating and discontinuing antibiotics for CABP among COVID-19 inpatients, we observed a reduction in antibiotic prescribing and DOT. The guideline also resulted in a significant increase in the rate of guideline-congruent empiric antibiotic initiation."

Int J Infect Dis: [Hydroxychloroquine as a primary prophylactic agent against sars-cov-2 infection: a cohort study](#) (01 June 2021)

"Highlights:

- > Largest cohort on hydroxychloroquine prophylaxis in COVID-19 to date.
- > All users of hydroxychloroquine in Denmark before the pandemic.
- > Hydroxychloroquine does not alter the risk of SARS-CoV-2.

Our study, which is the largest to investigate the primary prophylactic effect of hydroxychloroquine against SARS-CoV-2, does not support any prophylactic benefit of hydroxychloroquine in the prevention of infection with SARS-CoV-2."

PLoS Med: [Vitamin D and COVID-19 susceptibility and severity in the COVID-19 Host Genetics Initiative: A Mendelian randomization study](#) (01 June 2021)

"Why was this study done?

- > Vitamin D levels have been associated with COVID-19 outcomes in multiple observational studies, though confounders are likely to bias these associations.
- > By using genetic instruments that limit such confounding, Mendelian randomization studies have consistently obtained results concordant with vitamin D supplementation randomized trials. This provides a rationale to undertake vitamin D Mendelian randomization studies for COVID-19 outcomes.

What did the researchers do and find?

- > We used the genetic variants obtained from the largest consortium of COVID-19 cases and controls, and the largest study on genetic determinants of vitamin D levels.
- > We used Mendelian randomization to estimate the effect of increased vitamin D on COVID-19 outcomes, while limiting confounding.
- > In multiple analyses, our results consistently showed no evidence for an association between genetically predicted vitamin D level and COVID-19 susceptibility, hospitalization, or severe disease.

What do these findings mean?

- > Using Mendelian randomization to reduce confounding that has traditionally biased vitamin D observational studies, we did not find evidence that vitamin D supplementation in the general population would improve COVID-19 outcomes.
- > These findings, together with recent randomized controlled trial data, suggest that other therapies should be prioritized for COVID-19 trials."

Clin Infect Dis: [Outpatient Treatment of SARS-CoV-2 Infection to Prevent COVID-19 Progression](#) (28 May 2021)

"As of March 2021, COVID-19 has caused more than 123 million infections, and almost 3 million deaths worldwide. Dramatic advances have been made in vaccine development and non-pharmaceutical interventions to stop the spread of infection. But treatments to stop the progression of disease are limited. A wide variety of "repurposed" drugs explored for treatment of COVID-19 have had little or no benefit. More recently, intravenous monoclonal antibody (mAb) combinations have been authorized by the US FDA for emergency use (EUA) for outpatients with mild to moderate COVID-19 including some active against emerging

SARS-COV-2 variants of concern (VOC). Easier to administer therapeutics including intramuscular and subcutaneous mAbs and oral antivirals are in clinical trials. Reliable, safe, effective COVID-19 treatment for early infection in the outpatient setting is of urgent and critical importance. Availability of such treatment should lead to reduced progression of COVID-19."

JAMA Otolaryngol Head Neck Surg: [Association of Tracheostomy With Outcomes in Patients With COVID-19 and SARS-CoV-2 Transmission Among Health Care Professionals: A Systematic Review and Meta-analysis](#) (27 May 2021)

"Question Is tracheostomy associated with COVID-19 outcomes among patients or SARS-CoV-2 transmission among health care professionals (HCPs)?

Findings In this systematic review and meta-analysis, 69 nonrandomized studies including 4669 total patients were identified that evaluated tracheostomy in COVID-19. While the use of enhanced personal protective equipment in tracheostomy in patients with COVID-19 was associated with low SARS-CoV-2 transmission among HCPs and early tracheostomy was associated with reduced intensive care unit length of stay but not time to mechanical ventilation wean or decannulation, there was no difference in mortality between surgical and percutaneous tracheostomy.

Meaning This study suggests that tracheostomy is a relatively effective and safe treatment for patients with COVID-19 and also safe for the HCPs performing the procedures who are wearing personal protective equipment, but the conclusions are limited by the observational nature of included studies."

Lancet Respir Med: [Colchicine for community-treated patients with COVID-19 \(COLCORONA\): a phase 3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial](#) (27 May 2021)

"Potential clinical benefits of colchicine have been reported in observational studies and two small RCTs (including GRECCO) of patients admitted to hospital with COVID-19. In our COLCORONA double-blinded, placebo-controlled, randomised trial of 4488 non-hospitalised patients, including the 327 (7%) without a mandatory diagnostic test, the effect of colchicine on COVID-19-related clinical events was not statistically significant. Among the 4159 (93%) of patients with PCR-confirmed COVID-19, colchicine led to a lower rate of the composite of death or hospital admission than placebo.

Given the absence of orally administered therapies to prevent COVID-19 complications in community-treated patients, the burden on health-care systems caused by hospital admissions, and the benefit of colchicine in patients with PCR-proven COVID-19, we propose that colchicine is a safe and inexpensive anti-inflammatory agent that could be considered for use in those at risk of complications. Notwithstanding these considerations,

replication in other studies of patients who have positive PCR tests and have been treated in the community (such as the PRINCIPLE trial) is recommended. Additional trials such as the AGILE-ACCORD might enrich our therapeutic armamentarium to prevent COVID-19-related complications in ambulatory patients."

See also: [commentary](#)

Influenza Other Respir Viruses: [Admission respiratory status predicts mortality in COVID-19](#) (24 May 2021)

"COVID-19 has significant case fatality. Glucocorticoids are the only treatment shown to improve survival, but only among patients requiring supplemental oxygen. WHO advises patients to seek medical care for "trouble breathing," but hypoxemic patients frequently have no respiratory symptoms. Our cohort study of hospitalized COVID-19 patients shows that respiratory symptoms are uncommon and not associated with mortality. By contrast, objective signs of respiratory compromise—oxygen saturation and respiratory rate—are associated with markedly elevated mortality. Our findings support expanding guidelines to include at-home assessment of oxygen saturation and respiratory rate in order to expedite life-saving treatments patients to high-risk COVID-19 patients."

JAMA Intern Med: [Effectiveness of Tocilizumab in Patients Hospitalized With COVID-19: A Follow-up of the CORIMUNO-TOCI-1 Randomized Clinical Trial](#) (24 May 2021)

"This follow-up study of the CORIMUNO-TOCI-1 randomized clinical trial examines the association between survival and C-reactive protein levels in patients hospitalized with COVID-19 who were treated with tocilizumab."

JAMA Netw Open: [Medication Use Patterns in Hospitalized Patients With COVID-19 in California During the Pandemic](#) (21 May 2021)

"This cohort study examines trends in medication use among patients hospitalized for COVID-19–related treatment in a large US university health care system from the start of stay-at-home orders in March 2020 throughout the rest of the year....

This cohort study found that, early in the COVID-19 pandemic, antimicrobials azithromycin and hydroxychloroquine were each used in more than 40% of hospitalized patients. By June, use was below 30% and 5%, respectively. Enoxaparin use remained above 50% throughout 2020, perhaps because enoxaparin serves both for thrombosis prophylaxis and thrombophilia treatment triggered by COVID-19. Dexamethasone and remdesivir use grew substantially."

Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases

News in Brief

"'Better than the hospital': pandemic boosts care for serious illnesses at home" ([KHN](#)).

Peer-Reviewed Articles

Clin J Am Soc Nephrol: [Risk of COVID-19 Disease, Dialysis Unit Attributes, and Infection Control Strategy among London In-Center Hemodialysis Patients](#) (01 June 2021)

"Patients receiving in-center hemodialysis treatment face unique challenges during the COVID-19 pandemic, specifically the need to attend for treatment that prevents self-isolation. Dialysis unit attributes and isolation strategies that might reduce dialysis center COVID-19 infection rates have not been previously examined.

We explored the role of variables including community disease burden, dialysis unit attributes (size, layout) and infection control strategies, on rates of COVID-19 among patients receiving in center hemodialysis in London, UK, between March 2nd 2020 and May 31st 2020. The two outcomes were defined as (i) a positive test for infection or admission with suspected COVID19 and (ii) admission to the hospital with suspected infection. Associations were examined using a discrete-time multi-level time-to-event analysis.

Data on 5,755 patients, dialysing in 51 units were analysed. 990 (17%) tested positive and 465 (8%) were admitted with suspected COVID-19 between 2nd March and 31st May 2020. Outcomes were associated with age, diabetes, local community COVID-19 rates and dialysis unit size. Greater number of available side rooms and introduction of mask policies for asymptomatic patients were inversely associated with outcomes. No association was seen with sex, ethnicity, or deprivation indices nor with any of the different isolation strategies.

Rates of COVID-19 in the in center-hemodialysis population relate to individual factors, underlying community transmission, unit size and layout."

Open Forum Infect Dis: [Clinical features and outcomes of COVID-19 among people living with HIV in the United States: A multicenter study from a large global health research network \(TriNetX\)](#) (01 June 2021)

"HIV infection is a presumed risk factor for severe COVID-19, yet little is known about COVID-19 outcomes in people with HIV (PLW).

We used the TriNetX database to compare COVID-19 outcomes of PWH and HIV negative controls aged ≥ 18 years who sought care in 44 healthcare centers in the US from January 1 to December 1, 2020. Outcomes of interest were rates of hospitalization (composite of

inpatient non-intensive care (ICU) and ICU admissions), mechanical ventilation, severe disease (ICU admission or death) and 30-day mortality.

Of 297,194 confirmed COVID-19 cases, 1638 (0.6%) were HIV-infected, with > 83% on antiretroviral therapy (ART) and 48% virally suppressed. Overall, PWH were more commonly younger, male, African American or Hispanic, had more comorbidities, were more symptomatic, and had elevated procalcitonin and interleukin 6. Mortality at 30 days was comparable between the two groups (2.9% vs 2.3%; $p=0.123$); however, PWH had higher rates hospitalization (16.5% vs 7.6%, $p<0.001$), ICU admissions (4.2% vs 2.3%, $p<0.001$) and mechanical ventilation (2.4% vs 1.6%, $p<0.005$). Among PWH, hospitalization was independently associated with male gender, being African American, integrase inhibitor use and low CD4 count; whereas severe disease was predicted by older age [adjusted odds ratio (aOR) 8.33, 95% confidence interval (CI) (1.06, 50.00); $p=0.044$] and CD4 <200 cells/mm³ [aOR, 8.33, 95% CI (1.06, 50.00); $p=0.044$].

PWH had higher rates of poor COVID-19 outcomes but were not more at risk of death than non-HIV infected counterparts. Older age and low CD4 count predicted adverse outcomes."

JAMA Oncol: [Evaluation of Seropositivity Following BNT162b2 Messenger RNA Vaccination for SARS-CoV-2 in Patients Undergoing Treatment for Cancer](#) (28 May 2021)

"Question Do patients with cancer develop adequate antibody responses to messenger RNA SARS-CoV-2 vaccines?

Findings In this cohort study that included 102 patients with cancer who were receiving active treatment and 78 healthy controls, 92 patients with cancer (90%) and 100% of the controls were seropositive after the second messenger RNA BNT162b2 vaccine dose..

Meaning The findings of this study suggest that patients with cancer who are receiving active treatment and are at higher risk for severe COVID-19 disease respond well to messenger RNA SARS-CoV-2 vaccines and that vaccination of these patients should be seriously considered."

JAMA Oncol: [Difference in SARS-CoV-2 Antibody Status Between Patients With Cancer and Health Care Workers During the COVID-19 Pandemic in Japan](#) (28 May 2021)

"Question Are there differences in seroprevalence and antibody levels for SARS-CoV-2 between patients with cancer and health care workers (HCWs) during the COVID-19 pandemic in Japan?

Findings In this cross-sectional study including 500 patients with cancer and 1190 HCWs, the seroprevalence was 1.0% in patients and 0.67% in HCWs. However, the levels of IgG antibodies against nucleocapsid and spike protein were significantly lower in patients than in HCWs.

Meaning These findings indicate that seroprevalence was not different in patients with cancer compared with HCWs, but the immune response to SARS-CoV-2 may differ between patients with cancer and HCWs."

JAMA Cardiol: [Prevalence of Clinical and Subclinical Myocarditis in Competitive Athletes With Recent SARS-CoV-2 Infection: Results From the Big Ten COVID-19 Cardiac Registry](#) (27 May 2021)

"Question What is the prevalence of myocarditis in competitive athletes after COVID-19 infection, and how would different approaches to screening affect detection?

Findings In this cohort study of 1597 US competitive collegiate athletes undergoing comprehensive cardiovascular testing, the prevalence of clinical myocarditis based on a symptom-based screening strategy was only 0.31%. Screening with cardiovascular magnetic resonance imaging increased the prevalence of clinical and subclinical myocarditis by a factor of 7.4 to 2.3%.

Meaning These cardiac magnetic resonance imaging findings provide important data on the prevalence of clinical and subclinical myocarditis in college athletes recovering from symptomatic and asymptomatic COVID-19 infections."

JAMA Psychiatry: [Racial/Ethnic, Social, and Geographic Trends in Overdose-Associated Cardiac Arrests Observed by US Emergency Medical Services During the COVID-19 Pandemic](#) (26 May 2021)

"Question Can a national emergency medical services (EMS) database be used to rapidly surveil geographic, social, and overall trends in US overdose mortality?

Findings In this cohort study of 83.7 million EMS patient encounters, overdose-associated cardiac arrests rose about 40% nationally in 2020, with the largest increases among racial/ethnic minorities, in areas of socioeconomic disadvantage, and in Western states. High concordance was observed with provisional total overdose death figures through July 2020.

Meaning In this analysis, overdose deaths reached unprecedented levels during the pandemic, highlighting the need for investments in overdose prevention as an essential element of the COVID-19 response and postpandemic recovery, particularly for communities with greater vulnerability."

See also: JAMA Netw Open: [Measuring the Burden of Opioid-Related Mortality in Ontario, Canada, During the COVID-19 Pandemic](#) (26 May 2021)

JAMA Netw Open: [Association of Circulating Sex Hormones With Inflammation and Disease Severity in Patients With COVID-19](#) (25 May 2021)

"Question Are circulating sex hormones associated with disease severity in patients with COVID-19?

Findings In a cohort study of 152 patients with COVID-19, including 143 patients who were hospitalized, testosterone concentrations at presentation and on day 3 were inversely associated with disease severity and circulating inflammatory cytokine concentrations in men but not in women. Transcriptional profiling of circulating mononuclear cells revealed upregulation of hormone signaling pathways in patients requiring intensive care vs those with milder disease.

Meaning These findings suggest that low testosterone concentrations may play a mechanistic role in worse outcomes observed in men with COVID-19, underscoring the need for clinical trials to test this hypothesis."

Long COVID / Post-COVID Period

News in Brief

"After months of a racing heart and burning feet, A COVID long-hauler gets a diagnosis" ([NPR](#)).

"COVID long haulers illuminate overlooked medical condition — more evidence for POTS after SARS-CoV-2 infection is helping to raise awareness" ([Medpage](#)).

Commentary: "Count the cost of disability caused by COVID-19: Focusing only on cases and deaths hides the pandemic's lasting health burden on people, societies and economies" ([Nature](#)).

Peer-Reviewed Articles

BMJ Mil Health: [Rehabilitation post-COVID-19: cross-sectional observations using the Stanford Hall remote assessment tool](#) (26 May 2021)

"The multisystem COVID-19 can cause prolonged symptoms requiring rehabilitation. This study describes the creation of a remote COVID-19 rehabilitation assessment tool to allow timely triage, assessment and management. It hypothesizes those with post-COVID-19 syndrome, potentially without laboratory confirmation and irrespective of initial disease severity, will have significant rehabilitation needs.

Cross-sectional study of consecutive patients referred by general practitioners (April–November 2020). Primary outcomes were presence/absence of anticipated sequelae. Binary logistic regression was used to test association between acute presentation and post-COVID-19 symptomatology.

155 patients (n=127 men, n=28 women, median age 39 years, median 13 weeks post-illness) were assessed using the tool. Acute symptoms were most commonly shortness of breath (SOB) (74.2%), fever (73.5%), fatigue (70.3%) and cough (64.5%); and post-acutely, SOB (76.7%), fatigue (70.3%), cough (57.4%) and anxiety/mood disturbance (39.4%). Individuals with a confirmed diagnosis of COVID-19 were 69% and 63% less likely to have anxiety/mood disturbance and pain, respectively, at 3 months.

Rehabilitation assessment should be offered to all patients suffering post-COVID-19 symptoms, not only those with laboratory confirmation and considered independently from acute illness severity. This tool offers a structure for a remote assessment. Post-COVID-19 programmes should include SOB, fatigue and mood disturbance management."

JAMA Netw Open: [Assessment of the Frequency and Variety of Persistent Symptoms Among Patients With COVID-19: A Systematic Review](#) (26 May 2021)

"This systematic review uses data from cohort studies to examine the frequency, variety, and severity of persistent symptoms among individuals with previous COVID-19 infection....

Question What are the frequency and variety of persistent symptoms after COVID-19 infection?

Findings In this systematic review of 45 studies including 9751 participants with COVID-19, the median proportion of individuals who experienced at least 1 persistent symptom was 73%; symptoms occurring most frequently included shortness of breath or dyspnea, fatigue or exhaustion, and sleep disorders or insomnia. However, the studies were highly heterogeneous and needed longer follow-up and more standardized designs.

Meaning This systematic review found that COVID-19 symptoms commonly persisted beyond the acute phase of infection, with implications for health-associated functioning and quality of life; however, methodological improvements are needed to reliably quantify these risks."

Women's Health, Pregnancy, and Perinatal Care

Peer-Reviewed Articles

JAMA Netw Open: [Use of Electronic Medical Records to Estimate Changes in Pregnancy and Birth Rates During the COVID-19 Pandemic](#) (03 June 2021)

"Question Can electronic health care records be used to monitor and project changes in pregnancy and birth rates after the COVID-19 pandemic societal shutdown?

Findings In this cohort study of pregnancies within a large US university health care system, a model using electronic medical records (used retrospectively from 2017 and modeled

prospectively to 2021) projected an initial decline in births associated with the COVID-19 pandemic societal shutdown, predominantly related to fewer conceptions following the societal changes instituted to control COVID-19 spread. This decline was followed by a projected birth volume surge anticipated to occur in summer 2021.

Meaning These findings suggest that electronic medical records can be used to model and project birth volume changes and demonstrate that the COVID-19 pandemic societal changes are associated with reproductive choices."

Clin Infect Dis: [Risk factors for illness severity among pregnant women with confirmed SARS-CoV-2 infection – Surveillance for Emerging Threats to Mothers and Babies Network, 22 state, local, and territorial health departments, March 29, 2020 -March 5, 2021](#) (22 May 2021)

"Pregnant women with coronavirus disease 2019 (COVID-19) are at increased risk for severe illness compared with nonpregnant women. Data to assess risk factors for illness severity among pregnant women with COVID-19 are limited. This study aimed to determine risk factors associated with COVID-19 illness severity among pregnant women with SARS-CoV-2 infection.

Pregnant women with SARS-CoV-2 infection confirmed by molecular testing were reported during March 29, 2020–March 5, 2021 through the Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET). Criteria for illness severity (asymptomatic, mild, moderate-to-severe, or critical) were adapted from National Institutes of Health and World Health Organization criteria. Crude and adjusted risk ratios for moderate-to-severe or critical COVID-19 illness were calculated for selected demographic and clinical characteristics.

Among 7,950 pregnant women with SARS-CoV-2 infection, moderate-to-severe or critical COVID-19 illness was associated with age 25 years and older, healthcare occupation, pre-pregnancy obesity, chronic lung disease, chronic hypertension, and pregestational diabetes mellitus. Risk of moderate-to-severe or critical illness increased with the number of underlying medical or pregnancy-related conditions.

Older age and having underlying medical conditions were associated with increased risk of moderate-to-severe or critical COVID-19 illness among pregnant women. This information might help pregnant women understand their risk for moderate-to-severe or critical COVID-19 illness and inform targeted public health messaging."

Eur J Endocrinol: [Increased COVID-19 infections in women with polycystic ovary syndrome: a population-based study](#) (May 2021)

"Objective: Several recent observational studies have linked metabolic comorbidities to an increased risk from COVID-19. Here we investigated whether women with PCOS are at an increased risk of COVID-19 infection.

Design: Population-based closed cohort study between 31 January 2020 and 22 July 2020 in the setting of a UK primary care database (The Health Improvement Network, THIN).

Methods: The main outcome was the incidence of COVID-19 coded as suspected or confirmed by the primary care provider. We used Cox proportional hazards regression model with stepwise inclusion of explanatory variables (age, BMI, impaired glucose regulation, androgen excess, anovulation, vitamin D deficiency, hypertension, and cardiovascular disease) to provide unadjusted and adjusted hazard risks (HR) of COVID-19 infection among women with PCOS compared to women without PCOS.

Results: We identified 21 292 women with a coded diagnosis of PCO/PCOS and randomly selected 78 310 aged and general practice matched control women. The crude COVID-19 incidence was 18.1 and 11.9 per 1000 person-years among women with and without PCOS, respectively. Age-adjusted Cox regression analysis suggested a 51% higher risk of COVID-19 among women with PCOS compared to women without PCOS (HR: 1.51 (95% CI: 1.27-1.80), $P < 0.001$). After adjusting for age and BMI, HR reduced to 1.36 (1.14-1.63), $P = 0.001$. In the fully adjusted model, women with PCOS had a 28% increased risk of COVID-19 (aHR: 1.28 (1.05-1.56), $P = 0.015$).

Conclusion: Women with PCOS are at an increased risk of COVID-19 infection and should be specifically encouraged to adhere to infection control measures during the COVID-19 pandemic.

Significance statement: Women with polycystic ovary syndrome (PCOS) have an increased risk of cardio-metabolic disease, which have been identified as a risk factor for COVID-19. To investigate whether the increased metabolic risk in PCOS translates into an increased risk of COVID-19 infection, we carried out a population-based closed cohort study in the UK during its first wave of the SARS-CoV-2 pandemic (January to July 2020), including 21 292 women with PCOS and 78 310 controls matched for sex, age and general practice location. Results revealed a 52% increased risk of COVID-19 infection in women with PCOS, which remained increased at 28% above controls after adjustment for age, BMI, impaired glucose regulation and other explanatory variables."

Pediatric Population

News in Brief

About 2 weeks after the FDA gave EUA for the Pfizer vaccine in kids 12-17, Moderna says its vaccine is effective and plans to request EUA in early June ([NPR](#); see also: [Medpage Today article](#) and [Moderna press release](#)).

The AAP recommends that children (>2 years) should still wear face masks if they aren't fully vaccinated ([AAP](#)).

Mental Health

"New pediatricians are seeing few 'bread and butter' cases, but an influx of mental health crises" ([STAT](#)).

It's bad enough that Children's Hospital Colorado has declared a state of emergency over youth mental health ([CHC](#)).

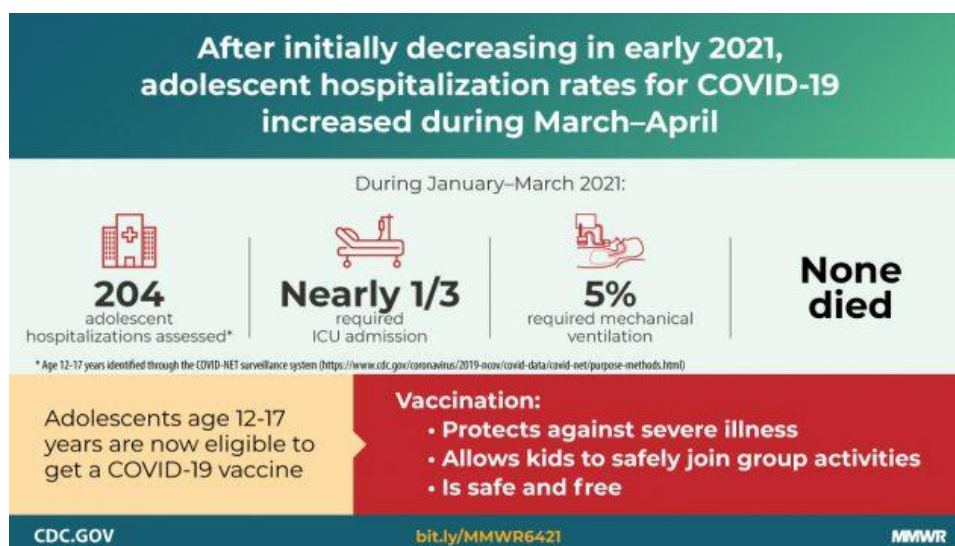
Peer-Reviewed Articles

MMWR: [Hospitalization of Adolescents Aged 12–17 Years with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, March 1, 2020–April 24, 2021](#) (04 June 2021)

"What is already known about this topic? Most COVID-19–associated hospitalizations occur in adults, but severe disease occurs in all age groups, including adolescents aged 12–17 years.

What is added by this report? COVID-19 adolescent hospitalization rates from COVID-NET peaked at 2.1 per 100,000 in early January 2021, declined to 0.6 in mid-March, and rose to 1.3 in April. Among hospitalized adolescents, nearly one third required intensive care unit admission, and 5% required invasive mechanical ventilation; no associated deaths occurred.

What are the implications for public health practice? Recent increased hospitalization rates in spring 2021 and potential for severe disease reinforce the importance of continued COVID-19 prevention measures, including vaccination and correct and consistent mask wearing among persons not fully vaccinated or when required."



Pediatrics: [30-Day Outcomes of Children and Adolescents With COVID-19: An International Experience](#) (28 May 2021)

"Objectives: To characterize the demographics, comorbidities, symptoms, in-hospital treatments, and health outcomes among children/adolescents diagnosed or hospitalized with COVID-19, and to compare them in secondary analyses with patients diagnosed with previous seasonal influenza in 2017-2018.

Methods: International network cohort using real-world data from European primary care records (France/Germany/Spain), South Korean claims and US claims and hospital databases. We included children/adolescents diagnosed and/or hospitalized with COVID-19 at age <18 between January and June 2020. We described baseline demographics, comorbidities, symptoms, 30-day in-hospital treatments and outcomes including hospitalization, pneumonia, acute respiratory distress syndrome (ARDS), multi-system inflammatory syndrome (MIS-C), and death.

Results: A total of 242,158 children/adolescents diagnosed and 9,769 hospitalized with COVID19, and 2,084,180 diagnosed with influenza were studied. Comorbidities including neurodevelopmental disorders, heart disease, and cancer were more common among hospitalized vs diagnosed with COVID-19. Dyspnea, bronchiolitis, anosmia and gastrointestinal symptoms were more common in COVID-19 than influenza. In-hospital prevalent treatments for COVID19 included repurposed medications (<10%), and adjunctive therapies: systemic corticosteroids (6.8%-7.6%), famotidine (9.0%-28.1%), and antithrombotics such as aspirin (2.0%-21.4%), heparin (2.2%-18.1%), and enoxaparin (2.8%-14.8%). Hospitalization was observed in 0.3% to 1.3% of the COVID-19 diagnosed cohort, with undetectable (N<5 per database) 30-day fatality. Thirty-day outcomes including pneumonia and hypoxemia were more frequent in COVID-19 than influenza.

Conclusions: Despite negligible fatality, complications including hospitalization, hypoxemia and pneumonia were more frequent in children/adolescents with COVID-19 than with influenza. Dyspnea, anosmia and gastrointestinal symptoms could help differentiate diagnoses. A wide range of medications was used for the inpatient management of pediatric COVID-19."

J Clin Invest: [Multisystem inflammatory syndrome in children is driven by zonulin-dependent loss of gut mucosal barrier](#) (25 May 2021)

"Weeks after SARS-CoV-2 infection or exposure, some children develop a severe, life-threatening illness called Multisystem Inflammatory Syndrome in Children (MIS-C). Gastrointestinal symptoms are common in MIS-C patients and severe hyperinflammatory response ensues with potential for cardiac complications. The cause of MIS-C has not previously been identified.

Here, we analyzed biospecimens from 100 children: 19 children with MIS-C, 26 with acute COVID-19, and 55 controls. Stool was assessed for SARS-CoV-2 by RT-PCR and plasma was assessed for markers of breakdown of mucosal barrier integrity, including zonulin. Ultrasensitive antigen detection was used to probe for SARS-CoV-2 antigenemia in plasma, and immune responses were characterized. As proof of concept, we treated a MIS-C patient with larazotide, a zonulin antagonist, and monitored impact on antigenemia and clinical response.

We showed that in MIS-C, prolonged presence of SARS-CoV-2 in the GI tract leads to release of zonulin, a biomarker of intestinal permeability, with subsequent trafficking of SARS-CoV-2 antigens into the bloodstream, leading to hyperinflammation. The MIS-C patient treated with larazotide displayed a coinciding decrease in plasma SARS-CoV-2 Spike antigen levels, inflammatory markers, and a resultant clinical improvement above that achieved with currently available treatments.

These mechanistic data of MIS-C pathogenesis provide insight into targets for diagnosing, treating, and preventing MIS-C, which are urgently needed for this increasingly common severe COVID-19-related disease in children."

Lancet Child Adolesc Health: [6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome \(PIMS-TS\) at a UK tertiary paediatric hospital: a retrospective cohort study](#) (24 May 2021)

"In this retrospective cohort study, we describe a range of outcomes in patients with PIMS-TS, including biochemical and functional outcomes measured up to 6 months as part of a multidisciplinary follow-up clinic. We found that whereas cardiac, gastrointestinal, renal, haematology, and otolaryngology outcomes largely resolved at 6 months, muscular fatigue and emotional lability were common. Long-term, serious end-organ damage occurred in some patients but was uncommon in this cohort. This analysis highlights the importance of physical rehabilitation and mental health provision for patients with PIMS-TS following discharge from hospital.

Our results can help to guide families and health-care providers about the natural history of PIMS-TS. Because PIMS-TS is a novel condition, long-term, holistic, and multidisciplinary follow-up of patients will be important."

MMWR: [Characteristics of COVID-19 Cases and Outbreaks at Child Care Facilities — District of Columbia, July–December 2020](#) (21 May 2021)

"What is already known about this topic? COVID-19 cases reported at child care facilities are correlated with level of community transmission.

What is added by this report? Among 469 child care facilities in the District of Columbia, 23.9% reported at least one COVID-19 case, and 5.8% reported outbreak-associated cases

during July 1–December 31, 2020. Among 319 cases, approximately one half were among teachers or staff members. Outbreak risk was increased in facilities operating <3 years, with symptomatic persons who sought testing ≥ 3 days after symptom onset, or with asymptomatic cases.

What are the implications for public health practice? Implementation and maintenance of multiple prevention strategies are important to reduce SARS-CoV-2 transmission in child care facilities and to facilitate a timely public health response to prevent outbreaks."

Impact on Healthcare Workers

Special Reports and Other Resources

GWU: [COVID-19 National Health Worker Survey \[pdf\]](#) (25 May 2021)

See also: [press release](#)

"This report summarizes results of a national COVID-19 health care worker (HCW) anonymous online survey conducted by students and staff with support from faculty mentors of the Department of Environmental and Occupational Health at The George Washington University Milken Institute School of Public Health. The survey was launched in May 2020 to capture the COVID-19 related workplace experiences of a group of HCWs, frontline US workers who have worked since the onset of the pandemic to provide care for millions of Americans. This report discusses survey responses of 1,200 HCWs collected during May and June 2020.

There are over 18 million HCWs in the US and HCWs on the frontlines of the COVID-19 pandemic have much to say about what should be done to prevent future COVID-19 exposures and infections. Unfortunately, their voices have often been unheard in the national COVID-19 response. The objective of this survey was to give voice to the experiences of these workers who are caring for and healing millions of people under extraordinary circumstances.

The following concerns were repeatedly mentioned in survey responses

- Frustration with unsafe working conditions, especially failed access to adequate personal protective equipment.
- Instances of retaliation and at times bullying for voicing their safety concerns to employers.
- Perceptions that employers prioritized hospital profits over worker safety and created an unhealthy work environment where workers felt devalued and threatened.

In their responses, survey participants asked for evidence-based protections, improved access to PPE, and greater respect and support from employers, researchers, and the general public."

Peer-Reviewed Articles

J Dent Res: [COVID-19: Seroprevalence and Vaccine Responses in UK Dental Care Professionals](#) (02 June 2021)

"Dental care professionals (DCPs) are thought to be at enhanced risk of occupational exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, robust data to support this from large-scale seroepidemiological studies are lacking. We report a longitudinal seroprevalence analysis of antibodies to SARS-CoV-2 spike glycoprotein, with baseline sampling prior to large-scale practice reopening in July 2020 and follow-up postimplementation of new public health guidance on infection prevention control (IPC) and enhanced personal protective equipment (PPE). In total, 1,507 West Midlands DCPs were recruited into this study in June 2020. Baseline seroprevalence was determined using a combined IgGAM enzyme-linked immunosorbent assay and the cohort followed longitudinally for 6 mo until January/February 2021 through the second wave of the coronavirus disease 2019 pandemic in the United Kingdom and vaccination commencement. Baseline seroprevalence was 16.3%, compared to estimates in the regional population of 6% to 7%. Seropositivity was retained in over 70% of participants at 3- and 6-mo follow-up and conferred a 75% reduced risk of infection. Nonwhite ethnicity and living in areas of greater deprivation were associated with increased baseline seroprevalence. During follow-up, no polymerase chain reaction–proven infections occurred in individuals with a baseline anti–SARS-CoV-2 IgG level greater than 147.6 IU/ml with respect to the World Health Organization international standard 20-136. After vaccination, antibody responses were more rapid and of higher magnitude in those individuals who were seropositive at baseline. Natural infection with SARS-CoV-2 prior to enhanced PPE was significantly higher in DCPs than the regional population. Natural infection leads to a serological response that remains detectable in over 70% of individuals 6 mo after initial sampling and 9 mo from the peak of the first wave of the pandemic. This response is associated with protection from future infection. Even if serological responses wane, a single dose of the Pfizer-BioNTech 162b vaccine is associated with an antibody response indicative of immunological memory."

J Am Dent Assoc: [COVID-2019 among dentists in the United States: A 6-month longitudinal report of accumulative prevalence and incidence](#) (01 June 2021)

"In 2020, the Centers for Disease Control and Prevention and the America Dental Association released COVID-19 infection control interim guidance for US dentists, advising

the use of optimal personal protection equipment during aerosol-generating procedures. The aim of this longitudinal study was to determine the cumulative prevalence and incidence rates of COVID-19 among dentists and to assess their level of engagement in specific infection control practices.

US dentists were invited to participate in a monthly web-based survey from June through November 2020. Approximately one-third of initial respondents (n = 785) participated in all 6 surveys, and they were asked about COVID-19 testing received, symptoms experienced, and infection prevention procedures followed in their primary practice.

Over a 6-month period, the cumulative COVID-19 infection prevalence rate was 2.6%, representing 57 dentists who ever received a diagnosis of COVID-19. The incidence rates ranged from 0.2% through 1.1% each month. The proportion of dentists tested for COVID-19 increased over time, as did the rate of dentists performing aerosol-generating procedures. Enhanced infection prevention and control strategies in the dental practice were reported by nearly every participant monthly, and rates of personal protection equipment optimization, such as changing masks after each patient, dropped over time.

US dentists continue to show a high level of adherence to enhanced infection control procedures in response to the ongoing pandemic, resulting in low rates of cumulative prevalence of COVID-19. Dentists are showing adherence to a strict protocol for enhanced infection control, which should help protect their patients, their dental team members, and themselves.

COVID-19 infections among practicing dentists will likely remain low if dentists continue to adhere to guidance."

Mental Health and Wellness

News in Brief

Mental health is for everyone, including pets: "6 tips for getting your dog ready for your return to the office" ([NPR](#)).

Long Reads

"What happens when Americans can finally exhale – The pandemic's mental wounds are still wide open" ([Atlantic](#)).

"The unique pain (and anger) of grieving someone who refused a COVID vaccine: 'Knowing there's something that was free, accessible, and could have prevented their death, it's heartbreaking.'" ([BuzzFeed](#))

"America has a drinking problem: A little alcohol can boost creativity and strengthen social ties. But there's nothing moderate, or convivial, about the way many Americans drink today" ([Atlantic](#)).

Take a Break

"Winners of the 2021 BigPicture Natural World Photography Competition" ([Atlantic](#)).

Sign of the Tides. Human / Nature Winner. Though a post-pandemic world is finally in sight, the scars of COVID-19 will live on for years to come—including those on our environment. Since the start of the pandemic, the production of single-use plastics skyrocketed, driven in part by the surge in epidemiologically necessary, but ecologically devastating, personal protective equipment. According to one study, 129 billion face masks and 65 billion



gloves were used globally each month during the pandemic, as much as 75 percent of which are likely to end up in landfills or the ocean. Much of that equipment—including this mask being investigated by a curious California sea lion—is made from durable plastics that take hundreds of years to break down. (Ralph Pace / BigPicture Natural World Photography Competition; used without permission.)

Peer-Reviewed Articles

BMJ Open: [Measuring the impact of COVID-19 on the quality of life of the survivors, partners and family members: a cross-sectional international online survey](#) (25 May 2021)

"Objective This study aimed to measure the impact of COVID-19 on the quality of life (QoL) of survivors and their partners and family members.

Design and setting A prospective cross-sectional global online survey using social media.

Participants Patients with COVID-19 and partners or family members (age ≥18 years).

Intervention Online survey from June to August 2020.

Main outcome measure The EuroQol group five dimensions three level (EQ-5D-3L) to measure the QoL of survivors of COVID-19, and the Family Reported Outcome Measure (FROM-16) to assess the impact on their partner/family member's QoL.

Results The survey was completed by 735 COVID-19 survivors (mean age=48 years; females=563) at a mean of 12.8 weeks after diagnosis and by 571 partners and 164 family members (n=735; mean age=47 years; females=246) from Europe (50.6%), North America (38.5%) and rest of the world (10.9%).

The EQ-5D mean score for COVID-19 survivors was 8.65 (SD=1.9, median=9; range=6–14). 81.1% (596/735) reported pain and discomfort, 79.5% (584/735) problems with usual activities, 68.7% (505/735) anxiety and depression and 56.2% (413/735) problems with mobility.

Hospitalised survivors (20.1%, n=148) and survivors with existing health conditions (30.9%, n=227) reported significantly more problems with mobility and usual activities ($p<0.05$), with hospitalised also experiencing more impact on self-care ($p\leq 0.001$).

Among 735 partners and family members, the mean FROM-16 score (maximum score=highest impact =32) was 15 (median=15, range=0-32). 93.6% (688/735) reported being worried, 81.7% (601/735) frustrated, 78.4% (676/735) sad, 83.3% (612/735) reported impact on their family activities, 68.9% (507/735) on sleep and 68.1% (500/735) on their sex life.

Conclusion COVID-19 survivors reported a major persisting impact on their physical and psychosocial health. The lives of their partners and other family members were also severely affected. There is a need for a holistic support system sensitive to the needs of COVID-19 survivors and their family members who experience a major 'secondary burden'."

Disparities and Health Equity

News in Brief

"How medical jargon can make COVID health disparities even worse" ([NPR](#)).

"Black residents now account for more than 8 in 10 D.C. coronavirus cases" ([WP](#)).

"A new tool tracks health disparities in the U.S. — and highlights major data gaps" ([STAT](#); check out [Health Equity Tracker](#)).

Want to know which hospitals are the most racially inclusive? There's a list for that ([Lown](#)).

The June issue of *AMA Journal of Ethics* focuses on transgenerational trauma, which may affect minority groups disproportionately and contribute to healthcare disparities ([AMA J Ethics](#)).

NMCP-Focused Information

If you attended the Command Grand Rounds about health disparities, you may be interested to know that NMCP Library Services has a variety of books on biases, health disparities, and racism in medicine. For example:

- *Biased: uncovering the hidden prejudice that shapes what we see, think, and do*
Jennifer L. Eberhardt (Fac Dev BF 575 P9 E34 2019)
- *The person you mean to be: how good people fight bias*
Dolly Chugh (CrewsLib BF 575 P9 C48 2018)
- *Just medicine: a cure for racial inequality in American health care*
Dayna Bowen Matthew (CrewsLib RA 448.4 M38 2018)
- *Black man in a white coat: a doctor's reflections on race and medicine*
Damon Tweedy (Fac Dev WZ 100 T84 2016)
- *Black and blue: the origins and consequences of medical racism*
John M. Hoberman (CrewsLib RA 563 H63 2012)
- *The organ thieves: the shocking story of the first heart transplant in the segregated south*
Chip Jones (CrewsLib RD 129.5 J66 2020)
- *Medical bondage: race, gender, and the origins of American gynecology*
Deirdre Cooper Owens (CrewsLib RG 67 C66 2017)
- *Medical apartheid: the dark history of medical experimentation on Black Americans from colonial times to the present*
Harriet A. Washington (CrewsLib R 853 W37 2006)
- *Race and medicine in nineteenth- and early-twentieth-century America*
Todd Lee Savitt (CrewsLib WA 11 AA1 S267r 2006)

[Search the library catalog](#) to view these and similar items from our collection.

Special Reports and Other Resources

AMA: [The AMA's strategic plan to embed racial justice and advance health equity](#) (May 2021)

See also: [STATnews article](#)

"The American Medical Association (AMA) is the nation's largest professional association of physicians. The AMA is a unifying voice and is the physicians' powerful ally in patient care. Fulfilling the AMA's mission to promote the art and science of medicine and the betterment of public health requires an unwavering commitment to equity and a comprehensive strategy for embedding racial and social justice within our organization and domains of influence.

Advancing health equity through the AMA's efforts entails a dedicated, coordinated and honest approach. It recognizes the harmful effects of the AMA's past and targets the systemic inequities in the health care system and other social institutions. And it charts a path toward a more promising and equitable future for all. ...

With the input of many both inside and outside of AMA, this strategic plan serves as a three-year roadmap to plant the initial seeds for action and accountability to embed racial justice and advance health equity for years to come. The AMA will initiate and aggressively push forward the following five strategic approaches:

1. Embed racial & social justice in AMA enterprise, culture, systems, policies, practices
2. Build alliances, share power with historically marginalized & minoritized physicians & other stakeholders
3. Ensure equitable structures & opportunities in innovation
4. Push upstream to address all determinants of health & root causes of inequities
5. Foster pathways for truth, racial healing, reconciliation and transformation for AMA's past"

RAND: [Sexual Assault of Sexual Minorities in the U.S. Military](#) (June 2021)

Note: While not focused on COVID-19, this report is included because of the topic and relevance to military concerns.

"Much of the focus of research on sexual assault in the military has been on the risk faced by women. However, in civilian populations, individuals who identify as lesbian, gay, and bisexual (LGB) are known to be at especially high risk for sexual assault.

In this report, RAND researchers examine evidence from the 2016 and 2018 Workplace and Gender Relations Survey of Active Duty Members (WGRA) survey to estimate the proportion of military sexual assaults that are against LGB service members and others who do not describe themselves as identifying as heterosexual. They find that assaults on the minority of service members who do not describe themselves as heterosexual constitute almost half of the military's sexual assault numbers. The authors discuss sexual assault risks for these individuals and recommend modifying prevention programs to better address a large and previously unquantified proportion of all military sexual assaults.

Key Findings

- Service members who identify as LGB or who do not indicate that they identify as heterosexual represented only 12 percent of the active component population in 2018, but accounted for approximately 43 percent of all sexually assaulted service members in that year.
- The 91 percent of men who identify as heterosexual only accounted for 52 percent of all men who were sexually assaulted over a one-year period; the remaining 9 percent of

men who did not indicate a heterosexual orientation accounted for 48 percent of all men who were sexually assaulted.

- The 77 percent of women who identify as heterosexual only accounted for 60 percent of all women who were sexually assaulted over a one-year period, while the remaining 23 percent of women who did not indicate a heterosexual orientation accounted for 40 percent of all women who were sexually assaulted.

Recommendations

- The Department of Defense could task the Office of People Analytics to perform detailed analyses of WGRA data to better understand circumstances and motivations around sexual assault of LGB service members.
- For development of effective prevention strategies, information about sexual assaults of sexual minorities could be incorporated into sexual assault prevention materials."

Peer-Reviewed Articles

NEJM: [Perspective: Institutional Problems, Individual Solutions — The Burden on Black Physicians](#) (29 May 2021)

"Medical institutions have the responsibility of addressing racism and continued mistrust within Black communities. Positioning Black physicians as the solution both deflects from this institutional responsibility and generates systemic problems for Black physicians who are already overburdened and underrepresented, hindering their career advancement. Amidst a steep crisis with a particularly devastating impact on Black communities, our solution to the acute racial inequities of the present must not exacerbate the racial inequities of the future."

JAMA Netw Open: [Factors Associated With Racial/Ethnic Group–Based Medical Mistrust and Perspectives on COVID-19 Vaccine Trial Participation and Vaccine Uptake in the US](#) (27 May 2021)

"Question Is there an association between race/ethnicity and rejection of COVID-19 vaccine trial participation and vaccine uptake in the US, and does racial/ethnic group–based medical mistrust mediate this association?

Findings In this survey study of 1835 adults in Michigan, Black participants reported the greatest medical mistrust among the racial/ethnic groups surveyed. Analysis of path models revealed significantly greater COVID-19 vaccine trial and uptake rejection among Black participants, which was partially mediated by medical mistrust.

Meaning The findings suggest that racial/ethnic group–based medical mistrust may partially explain the association between Black race/ethnicity and rejection of COVID-19

vaccine trial participation and uptake, potentially informing socially and culturally responsive efforts to promote COVID-19 vaccination in this group."

JAMA Netw Open: [Socioeconomic and Racial Inequities in Breast Cancer Screening During the COVID-19 Pandemic in Washington State](#) (24 May 2021)

"This cohort study investigates the rates of breast cancer screening before and during the COVID-19 pandemic among women in Washington State....

This study found a substantial overall decline in breast cancer screening in women living in Washington State during the COVID-19 pandemic, as well as inequities in this decline. This study has several limitations. First, the analyses were of aggregate data; we did not link individual records across years. Second, the demographic characteristics of this sample are slightly less diverse and more affluent than Washington State. Third, data reflect patient interactions with a single health care system; we weren't able to link these interactions to an underlying population base. However, the substantial drop in screenings in 2020 was not likely to be explained by a drop in underlying population base or eligibility; nor was it likely the result of a shift to different health care networks, given that this clinical network is one of the largest health care systems in Washington State."

Risk, Transmission, Exposure, and Testing

News in Brief

"What the science says about lifting mask mandates" ([Nature](#)).

When you want only the best, most photogenic puppies in medicine: "Faster than a PCR test: dogs detect Covid in under a second – study in London used six enthusiastic dogs in a double-blind trial" ([Guardian](#)).

Long read: "The 60-year-old scientific screwup that helped Covid kill: All pandemic long, scientists brawled over how the virus spreads. *Droplets! No, aerosols!* At the heart of the fight was a teensy error with huge consequences" ([Wired](#); may require free registration and login to read).

Special Reports and Other Resources

JHCHS: [School Ventilation: A Vital Tool to Reduce COVID-19 Spread](#) (26 May 2021)

"In this report, we consider the impact of the COVID-19 pandemic on children, families, and educators; review the evidence that improvements in ventilation reduces risks of disease transmission; and summarize current ventilation guidelines. While ventilation

improvements may often be perceived as a complicated and expensive investment, we demonstrate in a cost-effectiveness analysis comparing ventilation with enhanced ("deep") cleaning that ventilation improvements are a cost-effective public health measure. As new, potentially more transmissible variants of SARS-CoV-2 continue to emerge, broad improvements in indoor air quality are important for reducing transmission. Improvements to ventilation are a good use of the COVID-19 relief funds provided to K-12 schools....

A broad conclusion of this research is that the benefits to investing in healthy air in schools have the potential to outlast the COVID-19 pandemic. Improved ventilation may give children and school staff healthier indoor air quality for decades in the future, providing a healthier environment for nonpandemic times and potentially reducing risks in future infectious disease outbreaks."

Peer-Reviewed Articles

JAMA Intern Med: [Assessment of SARS-CoV-2 Reinfection 1 Year After Primary Infection in a Population in Lombardy, Italy](#) (28 May 2021)

"This cohort study examines the rate of SARS-CoV-2 reinfection among people in Lombardy, Italy, who previously recovered from COVID-19....

The study results suggest that reinfections are rare events and patients who have recovered from COVID-19 have a lower risk of reinfection. Natural immunity to SARS-CoV-2 appears to confer a protective effect for at least a year, which is similar to the protection reported in recent vaccine studies. However, the observation ended before SARS-CoV-2 variants began to spread, and it is unknown how well natural immunity to the wild-type virus will protect against variants."

Lancet Infect Dis: [Same-day SARS-CoV-2 antigen test screening in an indoor mass-gathering live music event: a randomised controlled trial](#) (27 May 2021)

"To our knowledge, this is the first randomised clinical trial that assesses the risk of COVID-19 transmission in an indoor mass-gathering live concert done under comprehensive safety measures, including same-day SARS-CoV-2 screening with antigen-detecting rapid diagnostic tests (Ag-RDTs), compulsory N95 face mask wearing, and optimised air ventilation. Participants could sing and dance in the concert hall room, and no physical distancing was recommended. None of the 465 participants became infected, compared with two out of 495 in the control arm.

Our study provides preliminary evidence on the effectiveness of same-day point-of-care screening with Ag-RDT, combined with face mask-wearing and active air ventilation, to create safe indoor environments with no need for physical distancing measures. Future

studies with a larger capacity of attendees and assistants, and done during periods of increased transmission of COVID-19 are warranted."

See also: [commentary](#)

Clin Infect Dis: [Serial intervals and case isolation delays for COVID-19: a systematic review and meta-analysis](#) (26 May 2021)

"Estimates of the serial interval distribution contribute to our understanding of the transmission dynamics of coronavirus disease 2019 (COVID-19). Here, we aimed to summarize the existing evidence on serial interval distributions and delays in case isolation for COVID-19.

We conducted a systematic review of the published literature and preprints in PubMed on two epidemiological parameters namely serial intervals and delay intervals relating to isolation of cases for COVID-19 until 22 October, 2020 following predefined eligibility criteria. We assessed the variation in these parameter estimates by correlation and regression analysis.

Of 103 unique studies identified on serial intervals of COVID-19, 56 were included providing 129 estimates and of 451 unique studies on isolation delays, 18 studies were included providing 74 estimates. Serial interval estimates varied from 1.0 to 9.9 days, while case isolation delays varied from 1.0 to 12.5 days which were associated with spatial, methodological and temporal factors. In mainland China, the pooled mean serial interval was 6.2 (range, 5.1-7.8) days before the epidemic peak and reduced to 4.9 (range, 1.9-6.5) days after the epidemic peak. Similarly, the pooled mean isolation delay related intervals were 6.0 (range, 2.9-12.5) days and 2.4 (range, 2.0-2.7) days before and after the epidemic peak, respectively. There was a positive association between serial interval and case isolation delay.

Temporal factors, such as different control measures and case isolation in particular led to shorter serial interval estimates over time. Correcting transmissibility estimates for these time-varying distributions could aid mitigation efforts."

Science: [Estimating infectiousness throughout SARS-CoV-2 infection course](#) (25 May 2021)

"Two elementary parameters for quantifying viral infection and shedding are viral load and whether samples yield a replicating virus isolate in cell culture. We examined 25,381 German SARS-CoV-2 cases, including 6110 from test centres attended by pre-symptomatic, asymptomatic, and mildly-symptomatic (PAMS) subjects, 9519 who were hospitalised, and 1533 B.1.1.7 lineage infections. The youngest had mean log₁₀ viral load 0.5 (or less) lower than older subjects and an estimated ~78% of the peak cell culture replication probability, due in part to smaller swab sizes and unlikely to be clinically relevant. Viral loads above 10⁹ copies per swab were found in 8% of subjects, one-third of whom were PAMS, with mean

age 37.6. We estimate 4.3 days from onset of shedding to peak viral load (8.1) and cell culture isolation probability (0.75). B.1.1.7 subjects had mean log₁₀ viral load 1.05 higher than non-B.1.1.7, with estimated cell culture replication probability 2.6 times higher."

EClinicalMedicine: [A population-based analysis of the longevity of SARS-CoV-2 antibody seropositivity in the United States](#) (24 May 2021)

"This cross-sectional study aimed to track population-based SARS-CoV-2 antibody seropositivity duration across the United States using observational data from a national clinical laboratory registry of patients tested by nucleic acid amplification (NAAT) and serologic assays. Knowledge of antibody seropositivity and its duration may help dictate post-pandemic planning.

Using assays to detect antibodies to either nucleocapsid (N) or spike (S) proteins performed on specimens from 39,086 individuals with confirmed positive COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR) from March 2020 to January 2021, we analyzed nationwide seropositivity rates of IgG up to 300 days following patients' initial positive NAAT test. Linear regression identified trends in seropositivity rates and logistic regression tested positive predictability by age, sex, assay type and days post-infection.

Seropositivity of IgG antibodies to both SARS-CoV-2 S and N-proteins followed a linear trend reaching approximately 90% positivity at 21 days post-index. The rate of N-protein seropositivity declined at a sharper rate, decaying to 68.2% [95% CI: 63.1-70.8%] after 293 days, while S-antibody seropositivity maintained a rate of 87.8% [95% CI: 86.3-89.1%] through 300 days. In addition to antigen type and the number of days post-positive PCR, age and gender were also significant factors in seropositivity prediction, with those under 65 years of age showing a more sustained seropositivity rate.

Observational data from a national clinical laboratory, though limited by an epidemiological view of the U.S. population, offer an encouraging timeline for the development and sustainability of antibodies up to ten months from natural infection and could inform post-pandemic planning."

JAMA Surg: [Assessing the Risk of SARS-CoV-2 Transmission via Surgical Electrocautery Plume](#) (21 May 2021)

"This quality improvement study used a nonhuman subject research approach to examine whether SARS-CoV-2 from aerosolized virus is present in and potentially transmissible from a electrocautery plume in surgery....

In this study, SARS-CoV-2 was not detectable in aerosol cautery plume generated from electrocautery under any of the conditions studied despite the high viral titers used. By mimicking surgery on a patient with a high SARS-CoV-2 load, there was a minimum of a 9 log reduction of viral RNA with any of the electrocautery methods. This suggests that

electrocautery smoke is an unlikely source of SARS-CoV-2 transmission for health care workers. This study is limited by the in vitro nature of the experiment, and collecting cautery plumes from airway surgery in patients with active SARS-CoV-2 would be definitive. Future work investigating the plume associated with lower-temperature thermal surgery (such as coblation or carbon dioxide laser) and different tissue substrates is warranted."

mSphere: [The Stability of Model Human Coronaviruses on Textiles in the Environment and during Health Care Laundering](#) (28 April 2021)

"Synthetic textiles such as polyester could potentially act as fomites of human coronaviruses, indicating the importance of infection control procedures during handling of contaminated textiles prior to laundering. This study provides novel evidence that human coronaviruses can persist on textiles for up to 3 days and are readily transferred from polyester textile to other surfaces after 72 h of incubation. This is of particular importance for the domestic laundering of contaminated textiles such as health care uniforms in the United Kingdom and United States, where there may be a risk of cross-contaminating the domestic environment. It was demonstrated that human coronaviruses are removed from contaminated textiles by typical domestic and commercial wash cycles, even at low temperatures without detergent, indicating that current health care laundering policies are likely sufficient in the decontamination of SARS-CoV-2 from textiles."

Reinfections, Coinfections, and Other Infectious Diseases

News in Brief

"As Covid dissipates in the U.S., cold and flu viruses may return with a vengeance" ([STAT](#)).

However... "A pandemic upside: The flu virus became less diverse, simplifying the task of making flu shots" ([STAT](#)).

And also this: "NIH begins Phase 1 clinical trial of NIAID's universal flu vaccine" ([HPN](#); [NIH press release](#)).

Long Reads

"The mRNA vaccine revolution is just beginning: mRNA brought us a Covid-19 vaccine in record speed. Next it could tackle flu, malaria or HIV" ([Wired](#)).

"Are U.S. officials under silent attack? The Havana Syndrome first affected spies and diplomats in Cuba. Now it has spread to the White House" ([New Yorker](#)).

Other Outbreaks

"China reports 1st known human case of H10N3 avian influenza" ([ONT](#)).

The CDC is investigating *Salmonella* outbreaks linked to backyard chickens ([CDC](#)) and raw frozen breaded stuffed chicken products ([CDC](#)).

I don't know... maybe the universe is telling us to avoid chickens.

Peer-Reviewed Articles

Lancet Microbe: [Co-infections, secondary infections, and antimicrobial use in patients hospitalised with COVID-19 during the first pandemic wave from the ISARIC WHO CCP-UK study: a multicentre, prospective cohort study](#) (02 June 2021)

"Microbiological characterisation of co-infections and secondary infections in patients with COVID-19 is lacking, and antimicrobial use is high. We aimed to describe microbiologically confirmed co-infections and secondary infections, and antimicrobial use, in patients admitted to hospital with COVID-19.

The International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) WHO Clinical Characterisation Protocol UK (CCP-UK) study is an ongoing, prospective cohort study recruiting inpatients from 260 hospitals in England, Scotland, and Wales, conducted by the ISARIC Coronavirus Clinical Characterisation Consortium. Patients with a confirmed or clinician-defined high likelihood of SARS-CoV-2 infection were eligible for inclusion in the ISARIC WHO CCP-UK study. For this specific study, we excluded patients with a recorded negative SARS-CoV-2 test result and those without a recorded outcome at 28 days after admission. Demographic, clinical, laboratory, therapeutic, and outcome data were collected using a prespecified case report form. Organisms considered clinically insignificant were excluded.

We analysed data from 48 902 patients admitted to hospital between Feb 6 and June 8, 2020. The median patient age was 74 years (IQR 59–84) and 20 786 (42.6%) of 48 765 patients were female. Microbiological investigations were recorded for 8649 (17.7%) of 48 902 patients, with clinically significant COVID-19-related respiratory or bloodstream culture results recorded for 1107 patients. 762 (70.6%) of 1080 infections were secondary, occurring more than 2 days after hospital admission. *Staphylococcus aureus* and *Haemophilus influenzae* were the most common pathogens causing respiratory co-infections (diagnosed ≤ 2 days after admission), with Enterobacteriaceae and *S aureus* most common in secondary respiratory infections. Bloodstream infections were most frequently caused by *Escherichia coli* and *S aureus*. Among patients with available data, 13 390 (37.0%) of 36 145 had received antimicrobials in the community for this illness episode before hospital admission and 39 258 (85.2%) of 46 061 patients with inpatient antimicrobial data received one or more antimicrobials at some point during their admission (highest for

patients in critical care). We identified frequent use of broad-spectrum agents and use of carbapenems rather than carbapenem-sparing alternatives.

In patients admitted to hospital with COVID-19, microbiologically confirmed bacterial infections are rare, and more likely to be secondary infections. Gram-negative organisms and *S aureus* are the predominant pathogens. The frequency and nature of antimicrobial use are concerning, but tractable targets for stewardship interventions exist."

Clin Infect Dis: [Coronavirus disease 2019 \(COVID-19\) Versus Influenza in Hospitalized Adult Patients in the United States: Differences in Demographic and Severity Indicators](#) (29 May 2021)

"Novel coronavirus disease 2019 (COVID-19) is frequently compared with influenza. The Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN) conducts studies on the etiology and characteristics of U.S. hospitalized adults with influenza. It began enrolling patients with COVID-19 hospitalizations in March 2020. Patients with influenza were compared with those with COVID-19 in the first months of the U.S. epidemic.

Adults aged ≥ 18 years admitted to hospitals in 4 sites with acute respiratory illness were tested by real-time reverse transcription polymerase chain reaction for influenza and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing COVID-19. Demographic and illness characteristics were collected for influenza illnesses during 3 seasons 2016–2019. Similar data were collected on COVID-19 cases admitted before June 19, 2020.

Age groups hospitalized with COVID-19 ($n = 914$) were similar to those admitted with influenza ($n = 1937$); 80% of patients with influenza and 75% of patients with COVID-19 were aged ≥ 50 years. Deaths from COVID-19 that occurred in younger patients were less often related to underlying conditions. White non-Hispanic persons were overrepresented in influenza (64%) compared with COVID-19 hospitalizations (37%). Greater severity and complications occurred with COVID-19 including more ICU admissions (AOR = 15.3 [95% CI: 11.6, 20.3]), ventilator use (AOR = 15.6 [95% CI: 10.7, 22.8]), 7 additional days of hospital stay in those discharged alive, and death during hospitalization (AOR = 19.8 [95% CI: 12.0, 32.7]).

While COVID-19 can cause a respiratory illness like influenza, it is associated with significantly greater severity of illness, longer hospital stays, and higher in-hospital deaths."

Clin Infect Dis: [Risk of reinfection after seroconversion to SARS-CoV-2: A population-based propensity-score matched cohort study](#) (27 May 2021)

"Serological assays detecting anti-SARS-CoV-2 antibodies are being widely deployed in studies and clinical practice. However, the duration and effectiveness of the protection conferred by the immune response remains to be assessed in population-based samples. To estimate the incidence of newly acquired SARS-CoV-2 infections in seropositive individuals

as compared to seronegative controls we conducted a retrospective longitudinal matched study.

A seroprevalence survey including a representative sample of the population was conducted in Geneva, Switzerland between April and June 2020, immediately after the first pandemic wave. Seropositive participants were matched one-to-two to seronegative controls, using a propensity-score including age, gender, immunodeficiency, BMI, smoking status and education level. Each individual was linked to a state-registry of SARS-CoV-2 infections. Our primary outcome was confirmed infections occurring from serological status assessment to the end of the second pandemic wave (January 2021).

Among 8344 serosurvey participants, 498 seropositive individuals were selected and matched with 996 seronegative controls. After a mean follow-up of 35.6 (SD 3.2) weeks, 7 out of 498 (1.4%) seropositive subjects had a positive SARS-CoV-2 test, of whom 5 (1.0%) were classified as reinfections. In contrast, the infection rate was higher in seronegative individuals (15.5%, 154/996) during a similar follow-up period (mean 34.7 [SD 3.2] weeks), corresponding to a 94% (95%CI 86% to 98%, $P < 0.001$) reduction in the hazard of having a positive SARS-CoV-2 test for seropositives.

Seroconversion after SARS-CoV-2 infection confers protection against reinfection lasting at least 8 months. These findings could help global health authorities establishing priority for vaccine allocation."

Infect Drug Resist: [Secondary Infections in Hospitalized COVID-19 Patients: Indian Experience](#) (24 May 2021)

"Critically ill coronavirus disease 2019 (COVID-19) patients need hospitalization which increases their risk of acquiring secondary bacterial and fungal infections. The practice of empiric antimicrobial prescription, due to limited diagnostic capabilities of many hospitals, has the potential to escalate an already worrisome antimicrobial resistance (AMR) situation in India. This study reports the prevalence and profiles of secondary infections (SIs) and clinical outcomes in hospitalized COVID-19 patients in India.

A retrospective study of secondary infections in patients admitted in intensive care units (ICUs) and wards of ten hospitals of the Indian Council of Medical Research (ICMR) AMR surveillance network, between June and August 2020, was undertaken. The demographic data, time of infection after admission, microbiological and antimicrobial resistance data of secondary infections, and clinical outcome data of the admitted COVID-19 patients were collated.

Out of 17,534 admitted patients, 3.6% of patients developed secondary bacterial or fungal infections. The mortality among patients who developed secondary infections was 56.7% against an overall mortality of 10.6% in total admitted COVID-19 patients. Gram-negative

bacteria were isolated from 78% of patients. *Klebsiella pneumoniae* (29%) was the predominant pathogen, followed by *Acinetobacter baumannii* (21%). Thirty-five percent of patients reported polymicrobial infections, including fungal infections. High levels of carbapenem resistance was seen in *A. baumannii* (92.6%) followed by *K. pneumoniae* (72.8%).

Predominance of Gram-negative pathogens in COVID-19 patients coupled with high rates of resistance to higher generation antimicrobials is an alarming finding. A high rate of mortality in patients with secondary infections warrants extra caution to improve the infection control practices and practice of antimicrobial stewardship interventions not only to save patient lives but also prevent selection of drug-resistant infections, to which the current situation is very conducive."

Lancet Infect Dis: [Safety and immunogenicity of a purified inactivated Zika virus vaccine candidate in healthy adults: an observer-blind, randomised, phase 1 trial](#) (18 May 2021)

"Zika virus, a flavivirus transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes, is associated with cases of congenital malformations and neurological complications. Absence of specific treatment makes a prophylactic Zika virus vaccine an unmet medical need. We assessed safety and immunogenicity of three doses of a purified, inactivated, Zika virus vaccine candidate in healthy flavivirus-naïve and flavivirus-primed adults.

This two-part, multicentre, observer-blind, randomised, placebo-controlled, phase 1 trial was done at seven medical clinics in the USA and two in Puerto Rico. Eligible participants were healthy adults aged 18–49 years. Participants were randomly assigned (1:1:1:1), using a sponsor-supplied randomisation scheme, to four groups to receive two intramuscular injections, 28 days apart, of saline placebo or TAK-426 containing 2 µg, 5 µg, or 10 µg antigen. Participants, investigators, and vaccine administering personnel were masked to group assignment. Part 1 of the study assessed flavivirus-naïve participants and part 2 assessed flavivirus-primed participants. The primary outcomes were safety, tolerability, and immunogenicity based on solicited local reactions and solicited systemic adverse events in the 7 days after each dose; unsolicited adverse events and serious adverse events in the 28 days after each dose; and geometric mean titres (GMTs) of neutralising anti-Zika virus antibodies at 28 days after the second dose. Safety assessments were done in all participants who received at least one dose of vaccine. Immunogenicity assessments were in the per-protocol set, comprising all participants who received at least one dose of vaccine and provided valid serology results at baseline and at least one post-vaccination timepoint, with no major protocol violations. The trial is ongoing and is registered at ClinicalTrials.gov (NCT03343626).

Between Nov 13, 2017, and Oct 24, 2018, 894 volunteers were screened and 271 enrolled (125 flavivirus-naïve and 146 flavivirus-primed participants). All TAK-426 doses were well

tolerated with no deaths, no vaccine-related serious adverse events, and similar rates of mainly mild to moderate adverse events. TAK-426 elicited dose-dependent increases in antibody GMTs in both flavivirus-naïve and flavivirus-primed participants. 28 days after dose 2, plaque-reduction neutralisation test GMTs in flavivirus-naïve participants were 1130 (95% CI 749–1703) in the 2 µg TAK-426 group, 1992 (1401–2833) in the 5 µg TAK-426 group, and 3690 (2677–5086) in the 10 µg TAK-426 group. In pairwise comparisons, responses after two vaccinations in the 10 µg group were significantly greater than in the 2 µg group (GMT ratio 3.27 [95% CI 1.98–5.39], $p < 0.0001$) and the 5 µg group (GMT ratio 1.85 [1.15–2.98], $p = 0.012$).

TAK-426 was well tolerated, with an acceptable safety profile, and was immunogenic in both flavivirus-naïve and flavivirus-primed adults. Based on the safety and immunogenicity profiles of all TAK-426 doses assessed, the 10 µg TAK-426 dose was selected for further clinical development."

Statistics

Global

04 JUN 2021: 172,245,410 confirmed cases and 3,703,795 deaths

United States

top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	33,327,911	3,792,962	2,959,205	2,329,867	2,103,768	1,383,647
Deaths	596,467	63,348	51,633	36,973	53,357	25,265

[JHU CSSE](#) as of 1000 EDT 04 June 2021

Virginia

	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	676,300	21,115	10,666	14,231	17,908	9,142	7,984	36,223
Hospitalizations	29,911	1,023	405	474	1,022	681	457	1,674
Deaths	11,222	301	178	233	264	200	191	407

[VA DOH](#) as of 1000 EDT 04 June 2021